Application No.: 09/945,258 2 Docket No.: 01034/100H570-US1

## AMENDMENTS TO THE CLAIMS

The following Listing of the Claims replaces all prior claims in the application.

- 1. (Withdrawn) A method for detecting a mutation in presentilin associated membrane protein (PAMP) associated with a neuropsychiatric or neurodevelopmental disorder, which method comprises detecting a variation in a sequence of a gene encoding PAMP obtained from an individual diagnosed with or suspected of having said disorder.
  - 2. (Withdrawn) The method of claim 1, wherein the disorder is schizophrenia.
- 3. (Withdrawn) A method for diagnosing individuals predisposed to or having a neuropsychiatric or neurodevelopmental disorder, which method comprises detecting a mutation in a gene encoding PAMP obtained from an individual.
  - 4. (Withdrawn) The method of claim 3, wherein the disorder is schizophrenia.
- 5. (Withdrawn) The method according to claim 3, wherein detection of the mutation comprises measuring a level of transcriptional activity of the gene.
- 6. (Withdrawn) The method according to claim 3, wherein detection of the mutation comprises measuring PAMP activity.
- 7. (Withdrawn) The method of claim 6, wherein said PAMP activity comprises PAMP expression level or activity of a product of a PAMP modified substrate.
- 8. (Withdrawn) A method for identifying a compound that is useful in treating a neuropsychiatric or neurodevelopmental disorder, which method comprises detecting modulation of PAMP expression in a transgenic animal that expresses PAMP, wherein the animal is contacted with the compound.
  - 9. (Withdrawn) The method of claim 8, wherein the disorder is schizophrenia.

Application No.: 09/945,258 Docket No.: 01034/100H570-US1

10. (Currently Amended) A method for identifying a candidate compound for treating a neuropsychiatric or neurodevelopmental disorder, which method comprises:

- (a) contacting a reconstituted system for measuring the interaction of a presentilin associated membrane protein (PAMP) activity and a PAMP substrate, comprising a PAMP, or a functional fragment thereof, and a PAMP substrate, with a test compound, the PAMP comprising an amino acid sequence at least 90% identical to at least one amino acid sequence selected from the group consisting of SEQ ID NO:14, SEQ ID NO:16 and SEQ ID NO:18; and
- (b) detecting a difference in the interaction of a PAMP activity and a PAMP substrate in the presence of the compound compared to the interaction of a PAMP activity and a PAMP substrate in the absence of the compound,

wherein the difference a decrease in the interaction of a PAMP activity and a PAMP substrate identifies the candidate compound.

- 11. (Original) The method of claim 10, wherein the disorder is schizophrenia.
- 12. (Withdrawn) A method for identifying a compound that is useful in treating a neuropsychiatric or neurodevelopmental disorder, which method comprises:
- (a) contacting a complex between a presentilin associated membrane protein (PAMP) and an agent, which agent provides a detectable conformational or functional change in said PAMP upon interaction with a substance being analyzed for activity against a neurodegenerative disease, with a test compound; and
  - (b) detecting a conformational or functional change in PAMP in the complex.
  - 13. (Withdrawn) The method of claim 12, wherein the disorder is schizophrenia.
- 14. (Withdrawn) The method of claim 12, wherein the test compound is a protein that interacts with PAMP.

- 15. (Withdrawn) A method for treating neuropsychiatric or neurodevelopmental disorder in a mammalian host which expresses at least one PAMP protein or a naturally occurring variant, which method comprises administering to the host an amount of compound effective to modulate PAMP expression in the host.
  - 16. (Withdrawn) The method of claim 15, wherein the disorder is schizophrenia.
- 17. (Previously Presented) The method of claim 10, wherein the PAMP amino acid sequence comprises a DYIGS amino acid sequence motif starting at a position corresponding to residue 336 of SEQ ID NO:14.
- 18. (Previously Presented) The method of claim 10, wherein the PAMP substrate is presentin 1.
  - 19. (Previously Presented) The method of claim 10, wherein the PAMP substrate is βAPP.
- 20. (Previously Presented) The method of claim 10, wherein the PAMP amino acid sequence comprises at least one amino acid sequence motif starting at a position corresponding to a residue of SEQ ID NO:14 selected from the group consisting of NKTA at residue 45, NATH at residue 55, NETK at residue 187, NGSA at residue 204, NQSQ at residue 417, NISG at residue 435, NNSW at residue 530, NTTY at residue 562, NLTG at residue 573, NLTR at residue 580, SGAG at residue 404, GCQSSI at residue 61, GNGLAY at residue 167, GAESAV at residue 294, GVVLAD at residue 438, TSR at residue 115, SSR at residue 340, SQK at residue 384, TRLD at residue 280, SFVE at residue 361, SIYD at residue 455, SSTE at residue 641, and combinations thereof.
- 21. (Previously Presented) The method of claim 20, wherein the PAMP amino acid sequence comprises the amino acid sequence motifs, starting at positions corresponding to residues of SEQ ID NO:14, NKTA at residue 45, NATH at residue 55, NETK at residue 187, NGSA at residue 204, NQSQ at residue 417, NISG at residue 435, NNSW at residue 530, NTTY at residue 562, NLTG at residue 573, NLTR at residue 580, SGAG at residue 404, GCQSSI at residue 61, GNGLAY at residue 167, GAESAV at residue 294, GVVLAD at residue 438, TSR at residue 115,

Docket No.: 01034/100H570-US1

Application No.: 09/945,258

SSR at residue 340, SQK at residue 384, TRLD at residue 280, SFVE at residue 361, SIYD at residue 455, and SSTE at residue 641.

5

- 22. (Previously Presented) The method of claim 21, wherein the PAMP has the amino acid sequence of SEQ ID NO:16.
- 23. (Previously Presented) The method of claim 21, wherein the PAMP has the amino acid sequence of SEQ ID NO:14.